SPINAL OSTEOPOROSIS, CAUSE UNKNOWN*

BY

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In this paper we propose to consider some normal features of the vertebral bodies and intervertebral discs, their modification in spinal osteoporosis, and the clinical and radiological consequences of these changes; then to consider the aetiology in the light of pathological investigations; and finally to discuss the treatment.

Anatomy

The adult vertebral bodies are composed of cancellous bone with a thin covering of cortical bone. This is largely replaced on each flat (upper or lower) surface by a plate of hyaline cartilage, which is conventionally regarded as part of the intervertebral disc. Sandwiched between two adjacent cartilage plates is the nucleus pulposus, which is enclosed by the annulus fibrosus. The annulus binds together the plates and adjacent vertebrae, and many of its fibres are continuous with the anterior and posterior common (longitudinal) ligaments. The three different elements of the intervertebral disc—the pair of cartilage plates, the nucleus pulposus, and the annulus—are shown diagrammatically in Fig. 1*a*.

Various changes which may occur in the discs are shown (in order of age of incidence) in Fig. 1*b-e*. Fig. 1*d* represents the disc as found in osteoporosis. The softened bone yields to the elastic tension of the nucleus pulposus, and the cartilaginous discs become indented into the vertebral bodies and thinned, so that the bodies become biconcave. Alternatively or additionally some vertebral bodies undergo gross collapse and become wedge-shaped. These changes are shown in Plate 1*a* and *b* from post-mortem specimens split longitudinally.

The microscopic changes are best seen by comparison with the appearances of a normal senile spine. Such is shown in Plate 1*IIa*, with the pathological section (Plate 1*IIb*) below it. Bony lamellae are extremely sparse and the thin cortex adjacent to the disc has practically disappeared (Plate 1*III*). The cartilage plate is thinned, and its structure shows changes consistent with those of compression or stretching. There is no evidence of excessive osteoclastic activity. The condition is, therefore, not one of excessive bone destruction. The bony lamellae, though sparse, are not encrusted with an osteoid stratum. The condition is, therefore, not one of diminished calcification (osteomalacia) but of diminished ossification. The absence of osteoid tissue shows that the condition is not osteomalacia, and therefore not due to vitamin D deficiency (Pommer, 1885; Maxwell and Turnbull, 1930; Maxwell, 1935).

Clinical Features

SEX AND AGE.—Sex and age incidence in 53 published cases are shown decennially and quinquennially in Fig. 2 (*a* and *b*), which suggests a greater, and generally slightly later, incidence in women than in men (Lance and others, 1938; Ravault and others, 1939; Meulengracht, 1939; Burrows and Graham, 1945).

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FIG. 1.—Diagrams of the adult intervertebral disc and its changes.

- (a) The normal disc.
- (b) Herniation of the nucleus pulposus through cartilage plate (often seen in adolescent kyphosis).
- (c) Rupture of the disc and retropulsion (a cause of sciatica).
- (d) Impression of the cartilage plates into the vertebral bodies in osteoporosis.
- (e) Degeneration of the discs (a cause of senile kyphosis).

FIG. 2.—Diagram to show the age incidence in and sex of 53 cases, our own and from the literature. Male patients are represented by cross-hatching. (By permission of the *Quarterly Journal of Medicine*.)

SYMPTOMS.—Symptoms are sometimes absent, but, when present, may be divided into chronic and acute. The principal chronic symptom is backache, more often lumbar than thoracic, and sometimes radiating to the buttocks and backs of the thighs or to the front of the chest or abdomen. The pain is usually worse with activity and relieved by rest. Other complaints sometimes found are stiffness, deformity (including diminution of stature) and a sensation of weakness of the back. Acute symptoms have occurred in about half our patients, usually as the first complaint. The patient may have a sudden, agonizing pain in the back when performing some trivial movement, such as bending down to pick something up or trying to open a stiff drawer. Sometimes something is heard or felt to snap in the back. Often the patient utters an involuntary cry. He may scarcely be able to move, and usually spends several days in bed, getting some relief from rest and warmth. The symptoms are thought to be due to a pathological fracture of a vertebra.

PHYSICAL SIGNS.—The physical signs are a rounded thoracic kyphosis (with a variably shaped lumbar spine) and, usually, considerable stiffness of the back. In advanced cases there may be indications of telescoping—shortening of the loins, with thoraco-lumbar folds and transverse abdominal furrow.

Radiological Changes

The changes are those of (1) osteoporosis, and (2) secondary vertebral deformities.

OSTEOPOROSIS.—A poorly-defined picture by a good radiographer suggests this. Often the vertebrae show less porosis in the neighbourhood of their upper and lower surfaces, so that these are portrayed by denser bands (Plate IVa). The distribution of the porotic changes through the skeleton is very interesting. The lumbar and thoracic parts of the spine show considerable alteration, often sufficient to cause deformity; the cervical spine, pelvis, ribs, clavicles, sternum, and scapulae may also be involved, but insufficiently to cause deformity; the other bones show no important change, though control radiographs of the hands may reveal some osteoporosis, suggesting that this is, in fact, generalized. In a normal adult the red marrow, which is very vascular, is almost confined to the bones of the spine, limb girdles, and thorax. It is these bones which are most affected by the porosis; the most accessible deposits of calcium are removed first.

DEFORMITY.—Material bony deformity occurs only in the most porotic vertebrae, namely the lumbar and thoracic. These undergo changes in shape in two ways: (i) moulding, due to the softness of the bone, (ii) pathological fracture because of the fragility of the bone. The changes in shape are (a) concavity, (b) wedging, (c) telescoping, or (d) combinations of all these. These changes are illustrated in Plates IV to VII.

Concavity.—The production of concavity of the upper and lower surfaces of the vertebral bodies has already been described. It is important not to mistake the radiological appearances of an obliquely viewed normal vertebra for those of a correctly centred biconcave one.

Wedging.—Wedging of vertebral bodies often conveys unmistakable evidence of pathological fracture.

Telescoping.—Telescoping, that is, compression of the whole vertebra, and not merely its body, is shown radiologically by approximation of the spinous processes without coincident lordosis. Plate VII *b* and *c* demonstrates progressive telescoping towards a condition called "kissing" spinous processes. There is often great variety of vertebral shape in the same spine.

Pathological Investigations and Aetiology

When, in 1939, we embarked on the investigation of a patient with osteoporosis of the spine, we were inclined to ascribe the great loss of calcium to a deficiency of vitamin D. Now, seven years later, our title shows that we are still ignorant of the cause. We have made the following investigations to try to discover it:

1. The blood count was normal except in two patients; one with pernicious anaemia and one with aplastic anaemia.
2. The renal function tests were normal except in one patient, who died of uraemia.
3. The serum cholesterol was raised in two patients with suspected Cushing's syndrome, i.e. 300 and 345 mg. per 100 c.cm.

PLATE Ia and b.—Longitudinally split necropsy specimens of spines in cases of osteoporosis. (By permission of the *Quarterly Journal of Medicine*.)

PLATE II.—(a) Section of part of normal senile spine. (b) Section of part of osteoporotic spine. (Half-tones in this and the following plate by permission of the *Quarterly Journal of Medicine*.)

PLATE IIIa and b.—Higher power of the last to show junction between bone and disc.

PLATE IV.—These two photographs, and those on Plates V and VI, show vertebral radiographic changes in various cases. (Plate IVb by permission of the *Quarterly Journal of Medicine*.)

PLATE V.

PLATE VI.

PLATE VII(a).—Vertebral radiographic changes in a case showing the opacities of bismuth injections for syphilis.
 (b and c).—Tracings of radiographs taken at an interval of 17 months. The approximation of the spinous processes in the second tracing reveals the telescoping of the vertebrae which has occurred. (By permission of the *Quarterly Journal of Medicine*.)
 (d).—Similar gross radiological changes in a case of Cushing's syndrome (pituitary type). (Dr. Gordon Holmes's and Mr. Broster's case.)

4. The stools appeared normal in all patients; and, in three in whom a chronic diarrhoea had been present at times, the amount of fat in the stools was within normal limits.

5. The serum calcium and phosphorus were estimated in seventeen out of the twenty cases. In seven cases the calcium was between 8 and 9 mg. per 100 c.cm., but in the others it was within normal limits (9 to 11 mg. per 100 c.cm.). The inorganic phosphorus was similarly within normal limits (3 to 5 mg. per 100 c.cm.) except in two patients, 1.8 mg. in one and 5.5 mg. per 100 c.cm. in the other; the latter patient ultimately died of renal failure.

6. The phosphatase was normal or just above normal in thirteen cases, and raised in four; in one, renal failure was present, and in the other three collapse of a vertebra had recently occurred.

These observations agree with those of other workers on the subject (Lance and others, 1938; Meulengracht, 1939; Black and others, 1941) and the normal serum phosphorus is against a lack of vitamin D.

7. We had intended to carry out calcium and phosphorus balances, but this was possible only in one patient before the war started. We did not consider that the diet and collection of stools and urine could be accurate when carried out in a busy E.M.S. hospital, because of the constant upsets due to air raids and the great excess of work due to the arrival of convoys. The one patient examined in 1939 was a young man who had had much bismuth injected for treatment of syphilis (Plate VIIa). A diet containing 1,000 mg. of calcium and 1,350 mg. of inorganic phosphorus was given under well controlled conditions. A negative calcium balance of 262 mg. was present, as was to be expected because of the lack of calcium in the bones. The phosphorus output was unfortunately not estimated. Extra vitamins (16,000 I.U. of vitamin D and 80,000 I.U. of vitamin A) were then given daily for the next 145 days, and the calcium and inorganic phosphorus balance estimated. The negative calcium balance of 262 mg. had been converted into a positive balance of 93 mg. a day, but a negative phosphorus balance of 40 mg. was found.

TABLE I
ESTIMATES OF CERTAIN MINERALS AND VITAMINS IN THE HABITUAL
DIETS OF SOME PATIENTS WITH OSTEOPOROSIS OF THE SPINE OF
UNKNOWN ORIGIN *

Patient	Sex	Age	Calcium mg.	Phosphor- ous mg.	Ca/P ratio	Vitamin A I.U.	Vitamin C mg.	Vitamin D I.U.
W S.	F.	38	1,407	—	—	1,447	29	144
E. P.	F.	44	200	689	(1:3.44)	—	—	Low
L. L.	F.	49	520	890	(1:1.71)	About 1,000	About 100	25
E. D.	F.	50	Low	735	—	—	—	—
M. S.	F.	56	<100	278	(>1:2.78)	—	—	Low
J. F.	F.	59	697	713	(1:1.02)	1,500	69	16
J. P.	F.	61	1,200	1,011.2	(1:0.84)	—	—	Low
M. E.	F.	63	419	678.4	(1:1.64)	3,026	48	36
K. M.	F.	67	400	531.7	(1:1.33)	—	—	Moderate
M. M.	F.	67	750	909	(1:1.2)	—	—	Low
B. J.	F.	68	591	626	(1:1.06)	2,900	14	76
R. H.	M.	44	1,200	—	—	—	—	—
H. P.	M.	53	270	553.5	(1:2.05)	—	—	Moderate
H. H.	M.	58	595	970	(1:1.63)	3,960	28	68
F. S.	M.	61	120	613 (?)	—	—	—	—
F. K.	M.	69	713	985	(1:1.38)	3,488	38	41
"Standard require- ment"			550	1,067	1:1.94	3,000 to 4,000	25 to 50	(?) 300 to 600

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TABLE 2

ESTIMATED MAXIMUM AND MINIMUM DAILY INTAKE OF CALCIUM
AND PHOSPHORUS UNDER CONDITIONS OF FOOD RATIONING,
1941-1943 *

	Calcium mg.		Phosphorous mg.	
	<i>Minimum</i>	<i>Maximum</i>	<i>Minimum</i>	<i>Maximum</i>
From rationed food	171.5	423.6	310.5	493.9
From unrationed food (no added calcium)	164.4	164.4	279.8	279.8
Total without added calcium	335.9	588	590.3	773.7
From 10 oz., national bread with added calcium	171	171	—	—
Total	506.9	759	590.3	773.7
"Standard requirement"	550		1,067	

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As this work was done early in our investigations it is little wonder that we ascribed the condition to lack of vitamin D, with its well-known action in causing a storage of calcium and phosphorus. We therefore treated all our patients with vitamin D, 10,000 to 16,000 I.U. a day for long periods. However, when we read the accounts of the patients with osteomalacia in Vienna by Hume and Nirenstein (1921) we realized that the clinical condition of our patients did not resemble that of the osteomalacia patients. In the latter condition there is pain on walking, and the shuffling gait is a prominent feature, and none of our patients had this. This made us very suspicious of the part played by a lack of vitamin D. Since we had found nineteen patients during the first three years of the war, while food was being rationed, we considered whether a lack of calcium and phosphorus in the diet of our patients could be a cause. With the aid of our dietitian, we therefore worked out the amount of calcium and phosphorus and vitamins A, D, and C in the diet, realizing that these were only approximate values (Table 1). This showed that, though eight out of sixteen patients were taking too little calcium (less than 550 mg.), eight were taking adequate amounts and three of these were taking much more than enough. The phosphorus, on the other hand, was deficient in the diets of all the fourteen patients in whom it was estimated (less than 600 mg. in three, between 600 and 800 in six, and 800 to 1,000 in five).

The figures for vitamin D are yet more difficult to estimate but certainly seemed low in nearly all cases, but we do not know how much is necessary nor how much is usually made by exposure to sunlight or sky-shine. The figures for vitamin A are within the usual limits. The ascorbic acid in seven cases seemed satisfactory, but it must be remembered that these are all calculated figures and we do not know how much was destroyed in the cooking.

We next considered whether the condition could be caused by the war-time

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dietary. Mrs. Newman, therefore, analysed the amount of calcium and phosphorus in the rationed foods during 1941 to 1943, with the results shown in Table 2. These showed that the calcium varied from 336 to 588 mg.; that is, from just over the standard figures to 214 mg. less than the standard. When calcium was added to the 85% extraction bread, the calcium figures varied from 43 mg. deficit to 200 mg. in excess, but it must be remembered that the phytic acid in the 85% extraction flour probably neutralized the additional calcium added. Hence the calcium obtained from the rationed food might have been sub-optimal. The phosphorus was definitely on the low side, ranging from a deficit of 477 to 294 mg. a day. The war-time diet was probably deficient in phosphorus rather than in calcium.

We have one piece of evidence for the hypothesis that lack of calcium and inorganic phosphorus may be an important factor. Dr. E. A. Carmichael asked us to see a patient in the National Hospital, Queen Square, who had very advanced osteoporosis of the spine. In the radiographs the vertebrae appeared like "ghosts", so little shadow did they cast. Dr. J. N. Cummings determined the calcium and phosphorus balance when the patient was given a diet containing 1,550 mg. of calcium and 1,200 mg. of phosphorus. This showed the astonishing result of a daily positive calcium balance of 750 mg. a day for six days, and positive phosphorus balance of 413 mg. a day. This patient was capable of storing calcium and phosphorus when she was given a diet high in calcium and phosphorus.

If diet has played any part, the condition is probably due to the long-standing choice of low calcium and low phosphorus diets, possibly accelerated by war-time restrictions.

So far the only evidence we have had as to causation is negative, but the death of two patients enabled us to answer one question. Prof. Geoffrey Hadfield found a complete lack of osteoid material in the sections of the spine, and this, as was pointed out to us by Dr. Donald Hunter (personal communication), proves that the condition is not due to lack of vitamin D. This finding confirms the opinion which we had formed on clinical grounds that the condition was not the same as osteomalacia, and therefore was not due to lack of vitamin D. This conclusion was only reached when one of us was away in the Navy, so that it was not possible to do any further work, but we had already considered other possibilities.

Thus ascorbic acid plays a very important part in the health and repair of bone (Bourne 1942-43*a*, 1942*b*). We had already guessed the amount of it taken in the diet, but we did not do saturation tests on these patients as soon as they came to hospital. We think this should be done in all cases, and might show that these patients were grossly unsaturated though not to an extent sufficient to cause symptoms of scurvy. It is possible that a long-continued state of vitamin C starvation might produce the osteoporosis. Prof. Hadfield decalcified the bone of one of our cases in some sections but failed to find any evidence of lack of ascorbic acid, such as the presence of precollagen. Thus there is no direct evidence for

this hypothesis. We hope, however, that further investigation may be made on this point.

Vitamin A is not believed to play any part in bone formation and we have found no evidence of the lack.

Another cause suggested has been habitual purgation (Meulengracht, 1938, 1939). Our patients did not indulge in this practice, and we find it hard to believe that it could have this effect.

Steatorrhoea, which undoubtedly causes bony changes like osteomalacia, was not present in any of our patients of this series, though we have seen one girl of seventeen whose femur was beginning to bend and the only factor present was a mild steatorrhoea. Large doses of vitamin D cured the condition of the femur.

So we ended our work with the negative conclusion that the condition of osteoporosis of the spine which existed in our patients was not caused by a lack of vitamin D. It may be due to a prolonged lack of calcium and phosphorus and vitamin C in the diet.

Diagnosis

Diagnosis depends upon (a) the clinical history and examination, (b) the insistence on radiography in cases of painful or kyphotic spine, (c) the ability to interpret radiographs in terms of normal and pathological anatomy, (d) the exclusion, largely by pathological methods, of known conditions giving closely similar or identical gross anatomical changes.

Differential Diagnosis

Three groups of cases need consideration: (1) those having a superficial clinical resemblance, (2) those having a superficial radiological resemblance, and (3) examples of known diseases causing identical or similar gross anatomical (and, therefore, clinical and radiological) changes.

DISEASES HAVING A SUPERFICIAL CLINICAL RESEMBLANCE

Fibrositis and arthritis are the most frequent erroneous diagnoses. Ankylosing spondylitis mimics by its stiff, rounded kyphosis. In spondylolisthesis the shortening of the trunk, with the consequent folds and furrows, resembles the telescoping which may occur in osteoporosis. Senile kyphosis due to disc degeneration (Fig. 1e) clinically resembles kyphosis due to osteoporosis. All these conditions are easily distinguished from spinal osteoporosis by radiology:

DISEASES HAVING A SUPERFICIAL RADIOLOGICAL RESEMBLANCE

Perhaps the commonest radiological error is to ascribe deformity of vertebral bodies in osteoporosis to metastatic neoplasms, especially as neighbouring vertebrae are often very unequally misshapen. Careful clinical and radiological consideration, supported perhaps by an estimation of the erythrocyte sedimentation rate, should settle the question. Traumatic fracture (and "Kümmell-Verneuil disease") may be distinguished by the history, the normality of the neighbouring vertebrae, and frequently narrowing of a contiguous disc.

KNOWN DISEASES CAUSING SIMILAR ANATOMICAL CHANGES

Diseases having gross spinal changes identical with or similar to those of the present condition may be grouped as follows:

Diseases involving bone marrow.—Similar gross spinal changes are found in myelomatosis, the leukaemias (especially leucopenic lymphocytic leukaemia), Hodgkin's disease, and Gaucher's disease. The urine must be tested for Bence-Jones protein and appropriate blood examinations made.

The osteomalacias.—Puerperal osteomalacia, hunger osteomalacia, and idiopathic steatorrhoea may all give spinal changes resembling those of osteoporosis macroscopically, though not microscopically. In osteoporosis, as in hunger osteomalacia, the severe pelvic deformity found in puerperal osteomalacia is absent. The waddling gait and severe bony tenderness of puerperal and hunger osteomalacia do not occur in osteoporosis.

Endocrine disturbances.—Similar gross spinal changes are found in the osteoporosis of hyperparathyroidism, hypopituitarism, and Cushing's syndrome (Plate VII*d*).

Fragilitas ossium.—The bones may be soft as well as fragile; consequently, the spinal changes of osteoporosis may occur. The history of fractures in youth, the frequent familial affection, and the blue sclerotics and sometimes otosclerosis make the diagnosis easy.

Treatment

LOCAL.—Nearly every patient was provided with, and habituated to a plaster bed. Most of them were fitted also with a spinal support of the Fisher type; if the condition was less severe a corset with posterior steel stiffening was fitted.

GENERAL.—The diet has been adjusted, and varying amounts of calcium, phosphorus, and vitamin D have been given.

The calcium salt which we prefer is the phosphate, not only because it provides phosphorus, but also because of its reasonably high calcium content (33%, compared with 13% in the lactate and 9% in the gluconate). The dosage used was 1 g. (gr. 15) three times a day. We have given up to 30,000 I.U. of vitamin D, but now that we know that the present condition differs from osteomalacia we are inclined to consider this dosage unnecessarily large, though we continue to give 5,000 to 10,000 I.U. daily as it may aid absorption of the calcium and phosphorus.

RESULTS OF TREATMENT

With the exception of the fatal cases, the patients all improved subjectively, the pain becoming relieved or substantially improved. At first we ascribed this to the local treatment, but we soon confirmed Meulengracht's observation of improvement with medication alone. The clinical improvement was not accompanied by any material increase in calcification as shown by radiographs repeated over periods of many months.

Conclusion

We have here a condition affecting adults above the age of 30—mainly women between 55 and 80, but also men, commonly between 40 and 70.

The condition is an osteoporosis from deficient ossification.

The cause of the deficient ossification is unknown, but it may perhaps be related to long-continued slight deficiency of such dietary constituents as calcium, phosphorus, and ascorbic acid; it is not due to vitamin D deficiency.

Although generalized osteoporosis can sometimes be demonstrated, a material degree of porosis is confined to those bones which, in the adult, contain red marrow, namely those of the spine, limb girdles, and thoracic cage. Only the lumbar and thoracic vertebrae undergo sufficient porosis to suffer material deformity.

The symptoms, signs, and radiographic appearances are explicable in terms of the plasticity and fragility of the lumbar and thoracic vertebrae.

Similar spinal deformities are found in known diseases causing osteoporosis and in osteomalacia.

With calcium medication the symptoms improve, but there is little or no demonstrable improvement in calcification.

We should like to acknowledge that we are presenting the work of many, some of whose names we have recorded elsewhere. We owe a particularly great debt to Prof. Geoffrey Hadfield, Dr. W. W. Kay, and Dr. Donald Hunter. Many of the figures are reproduced by kind permission of the Editor of the *Quarterly Journal of Medicine*.

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